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Kaposiform Hemangioendotelioma with Kasabach-Merritt Syndrome Treated With Propranolol and Vincristine

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Abstract: ***Aims:*** ***To demonstrate the efficacy of treatment with propranolol and vincristine in a case with kaposiform hemangioendothelioma and Kasabach-Merrit syndrome (KMS).*** ***Materials and Methods: This is a retrospective case report of a 5 month old girl admitted to our hospital because of a progressive purple, indurated large cutaneous lesion on her right upper anterior-posterior thoracic portion which extends toward neck. Laboratory evaluations showed thrombocytopenia, coagulopathy with a low fibrinogen and a high D-dimer plasma level. The clinical and laboratory investigations suggested the diagnosis of KHE with KMP. We started prednisone 4mg/kg/d and propranolol 1mg/kg/d and thereafter vincristine 0.05 mg/kg/P, once a week.*** ***Results : A dramatically clinical decrease of the lesion was seen during treatment with prednisone and propranolol but with very low platelet count and massive bleeding.Treatment with vincristine achieved a complete normalization of the platelet count. Neither regrowth of the tumor has been observed until now.*** ***Conclusion: Propranolol and vincristine seems to be an important addition for the life-threatening condition of KHE with KMS. We concluded that effect of propranolol was solely on the KHE and vincristine showed extraordinary effect on KMS, which need to be communicated in the treatment for future patients.***

Keywords: KHE-Kaposiform Hemangioendotelioma, KMS- Kasabach-Merritt Syndrome, prednisone, propranolol, vincristine

1. Introduction

Kaposiform hemangioendothelioma (KH) is a rare, locally aggressive vascular proliferation that occurs almost exclusively in infants and adolescents. It most commonly arises as a superficial or deep soft tissue mass of the extremities[1,] but locations in the neck, face, thorax, and retroperitoneum are also described in the literature. Clinical presentation is variable and depends on its location and size and the development of Kasabach-Merritt syndrome that may lead to thrombocytopenia and consumptive coagulopathy. In symptomatic KHE, associated with KMP, aggressive treatment is indicated. In deep and large lesions, however, surgical excision is either dangerous, because of bleeding risk or impossible, because of the size or location of the tumor. In these cases, several nonsurgical treatments have been shown to be successful. Medical therapies include systemic corticosteroids, vincristine (VCR), a-interferon (IFN), cyclophosphamide, rapamycin, and more recently, propranolol.

The literature regarding the use of these agents is limited, and there are no prospective studies that examine the efficacy and toxicities associated with their use in the setting of KMP. Oftentimes multimodal therapy is required. We report a case with KHE and KMP, in which we followed two lines of treatment: first line of treatment prednisone with propranolol and second line of treatment courses of weekly vincristine. Possibly, this is the start of a hopeful new approach in this severe, life-threatening condition.

2. Case Presentation

A 5-month-old girl was admitted to our hospital because of progressive violaceous, indurated large cutaneous lesion on her right upper antero-posterior thoracic portion which extends toward right neck , non pulsatile with local heat and forced position of the head on the left. Edema in this area extended on the face and right arm (Fig.1). Laboratory evaluations showed a hemoglobin level of 10.5 g/dL and thrombocytopenia (27 x 10^3/mL). Furthermore, a coagulopathy was seen with a fibrinogen level of 34.7 mg/dL (reference range, 200-400 mg /dL) and a D-dimer plasma level of 36.489 ng/ml (normal 0-500 ng/ml) .

Figure 1: Age 5 months, just before treatment with prednisone, propranolol and vincristine.

Despite giving platelet mass and vitamin K(Phytonadione**)** these parameters were not improved. Lack of hemorrhagic phenomena in other body sites and a normal bone marrow aspiration excluded a primary problem of coagulation. In these conditions, clotting disorder and thrombocytopenia appears to be secondary from local consumption. From imaging examinations resulted: no cavity with blood, no exit of the contrast from blood vessels, no expansion of veins filled with material inside to suggest for formation of thrombi.There was enlargement of subcutaneous soft tissues of the neck, clinically compatible with a vascular tumor, called kaposiform hemangioendothelioma which in our case was probably associated with the syndrome called Kasabach-Merritt syndrome with severe thrombocytopenia and consumption coagulopathy .

The clinical findings and laboratory investigations strongly suggested the diagnosis of KHE with KMP. Biopsy of the tumor was not attempted at this time because of the potential risk for hemorrhage. Following clinical diagnosis, we started prednisone 4mg/kg/d and propranolol (1mg/kg/d) in 2 divided doses (Fig.2), monitoring blood pressure, heart rate, and fasting glucose levels.

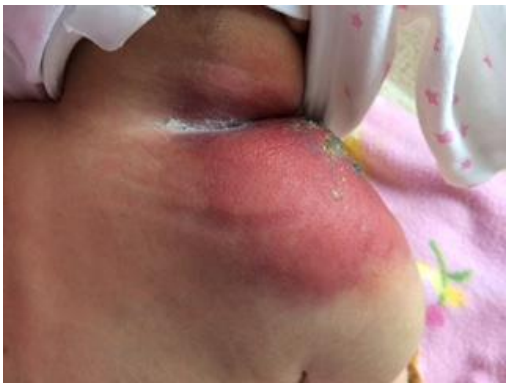

Figure 2: 4 weeks after starting prednisone and propranolol

During this therapy the lesion became softer, but the platelet counts remain low. On account of the low platelet count, our multidisciplinary group could not justify therapy with experimental propranolol anymore. Therefore, after mature consideration, we switched to another therapeutic regimen vincristine 0.05 mg/kg. After 6 courses of vincristine therapy, a normalization of the platelet count and an ongoing dramatically clinical decrease of the lesion were seen. (Fig.3).

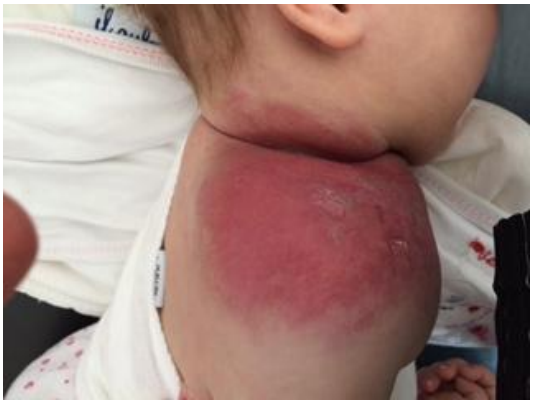

Figure 3: After 6 weeks treatment with vincristine

A total of 16 doses of vincristine was administered (0.05 mg/kg wk,once a week), (Fig.4).

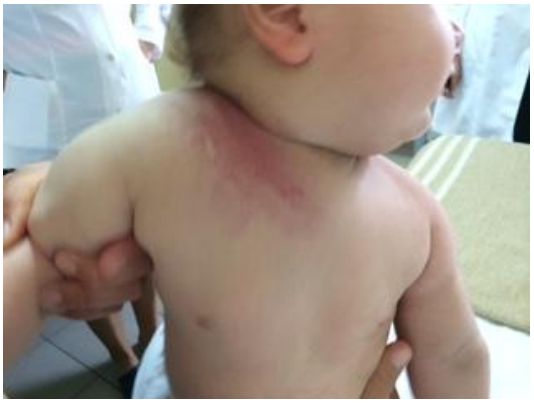

Figure 4: After 16 week's treatment with vincristine

The histopathological examination of the lesions highlighted the proliferation of small capillary vessels and dissection of them in derma. Immunohistochemistry examination was done with Ventana Benchmark XT antibodies, resulted: CD34 (+), Ki67 (variable from 2-50%), Actin (+), p53 (+rare). Immunohistochemistry of the lesion were consistent with Kassabach-Merrit Syndrome and confirmed the clinical diagnosis (Fig 5).

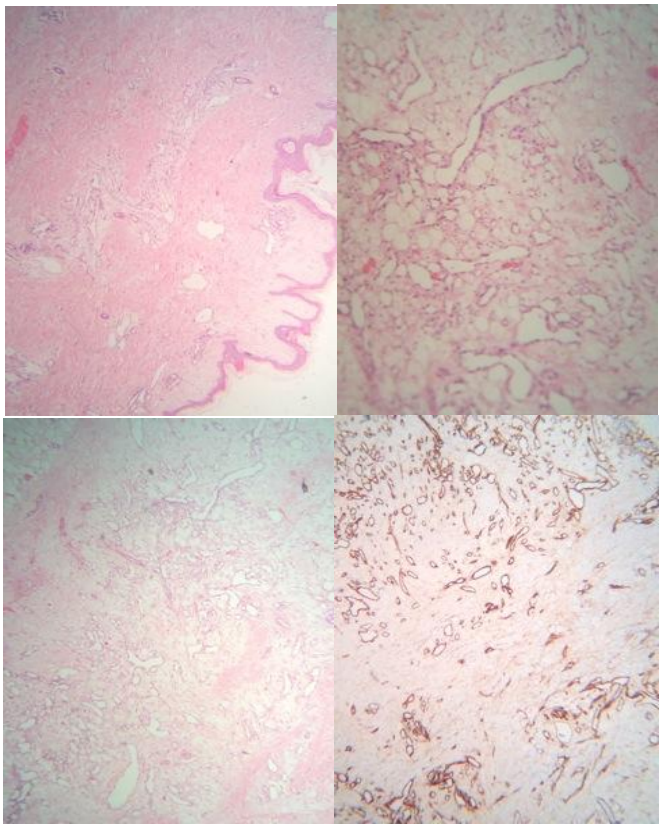

Figure 5: The histopathological examination of the lesions observed proliferation of small capillary vessels and dissection of them in derma. Immunohistochemistry examination were done with Ventana Benchmark XT, antibodies resulted: CD 34 (+) (tumour cells positive for vascular endothelial marker), Ki67 (variable from 2-50%), Actin (+), p53 (+ rare).

Neither regrowth of the tumor nor hematologic abnormalities has been observed until now. The hematologic parameters are being monitored at regular intervals to detect any late relapses of KHE paper. Format the page as two columns:

3. Discussion

KHE with KMP is a potentially life-threatening vascular abnormality that requires aggressive treatment. Spontaneous regression of these tumors is rare.[2]Various medical treatments such as steroid, IFN-a, propranolol and/ or chemotherapy that includes vincristine, adriamycin, and cyclophosphamide have been used because complete resection is impossible.[4,5,6,7]

Although steroid can be used as the first-line treatment, a previous study showed that there were various treatment responses to steroid: total failure (30%), excellent, dramatic, rapid improvement (30%), and a moderate to doubtful response (40%).[8]

In our case, therapy with steroid showed a moderate to doubtful response. In the literature, there are reports of propranolol in KHE and/or KMP with suspicion whether the effect of propranolol is solely on the underlying KHE (with a secondary beneficial effect on KMP) or probably on both aspects of the condition.[3] Therapy with propranolol in our case reduced the dimensions of the lesion and made it softer but it could not be justified anymore after 45 days of use because of the life-threatening hematologic parameters. Vincristine is often used to treat infantile hemangioendotelioma (IHE), as a single or combination agents.[2,4,9,10] Some reports have shown that combination treatment improved the treatment efficacy.[4,10,11]
Because of the slow and unpredictable response to therapy with a single drug, there is a tendency to administer several drugs in combination.[10]

Another report showed that the key to correct the thrombocytopenia in IHE with KMS is to treat the tumor that is responsible for platelet trapping.[10] Therefore, vincristine was added after treatment with propranolol in our case report.. Although in the literature, the average treatment duration of vincristine is 22 weekly courses,[12] in our patient a treatment period of only 16 weeks was necessary to establish hematologic parameters.

4. Conclusion

Propranolol and vincristine seems to be an important addition to the suboptimal therapeutic arsenal for the life-threatening condition of KHE with KMP. The effect of propranolol in our case report was solely on the underlying KHE and vincristine showed beneficial effect on KMP. Obviously, more experience with propranolol and vincristine in the treatment of KHE with KMP is necessary; however, the extraordinary effects in this case need to be communicated in this phase and propranolol and vincristine should be considered in the treatment for future patients with KHE and KMP.

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